UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,223	07/30/2003	Francis Michon	20695C-001410US	8301

65989 7590 06/05/2008

KING & SPALDING
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-4003

EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
06/05/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

usptomailnyc@kslaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/630,223	MICHON ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above claim(s) *22-41, 47-51 and 53-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,42-46 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed on 10/29/07 has been entered.

Applicants' Amendment

2) Acknowledgment is made of Applicants' amendment filed 10/29/07 in response to the final rejection mailed 07/27/07.

Status of Claims

3) Claims 1-4, 6, 10, 42 and 52 have been amended via the amendment mailed 10/27/07.

Claims 1-55 are pending.

Claims 1-11, 42-46 and 52 are under examination.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

5) The rejection of claims 1, 5, 6, 11 and 42-44 made in paragraph 10 of the Office Action mailed 10/23/06 and maintained in paragraph 11 of the Office Action mailed 07/27/07 under 35 U.S.C. § 102(b) as being anticipated by Michon *et al.* (*In*: *Streptococci and the Host*. (Ed) Horaud *et al*. Plenum Press, New York, pages 847-850, 1997) (Michon *et al*., 1997), is withdrawn in light of Applicants' amendment to the claims and/or the base claim(s).

6) The rejection of claims 1, 2, 5, 6, 10, 11 and 42-44 made in paragraph 11 of the Office Action mailed 10/23/06 and maintained in paragraph 12 of the Office Action mailed 07/27/07 under 35 U.S.C. § 102(b) as being anticipated by Paoletti *et al.* (*Infect. Immun*. 62: 3236-3243, 1994 – Applicants' IDS), is withdrawn in light of Applicants' amendment to the claims and/or the base claim(s).

7) The rejection of claims 9 and 52 made in paragraph 13 of the Office Action mailed 10/23/06 and maintained in paragraph 13 of the Office Action mailed 07/27/07 under 35 U.S.C. § 103(a) as being unpatentable over Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994 – Applicants' IDS) as applied to claims 6 and/or 1 above, and further in view of Wang *et al.* (*PNAS* 95: 6584-6589, 1998), is withdrawn in light of Applicants' amendment to the claims and/or the base claim(s).

8) The rejection of claims 2, 3, 7, 8, 45 and 46 made in paragraph 14 of the Office Action mailed 10/23/06 under 35 U.S.C. § 103(a) as being unpatentable over Michon *et al.* (*In*: *Streptococci and the Host.* (Ed) Horaud *et al.* Plenum Press, New York, pages 847-850, 1997) (Michon *et al.*, 1997) as applied to claims 6, 1 and 42 above and further in view of Michon *et al.* (US 6,602,508) ('508) and Laude-Sharp *et al.* (*In*: *Abstracts of the 97th General Meeting of the American Society for Microbiology*, Miami Beach, FL, page 251, # E-62, 1997), is withdrawn in light of Applicants' amendment to the claims and/or the base claim(s) in light of Applicants' amendment to the claims and/or the base claim(s).

9) The rejection of claim 1 and those dependent therefrom made in paragraph 16 of the Office Action mailed 07/27/07 under 35 U.S.C. § 112, first paragraph, rejected under 35 U.S.C § 112, first paragraph, as containing new matter, is withdrawn in light of Applicants' amendment to the claims and/or the base claim. A modified rejection is set forth below to address the claims as amended.

10) The rejection of claim 52 made in paragraph 17 of the Office Action mailed 07/27/07 under 35 U.S.C. § 112, first paragraph, as containing new matter, is withdrawn in light of Applicants' amendment to the claim and/or the base claim. A modified rejection is set forth below to address the claim as amended.

11) The rejection of claim 1 made in paragraphs 18(a), 18(b), 18(c) and 18(d) of the Office Action mailed 07/27/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

12) The rejection of claim 42 made in paragraph 18(d) of the Office Action mailed 07/27/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

13) The rejection of claims 2-4 made in paragraph 18(e) of the Office Action mailed 07/27/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

14) The rejection of claims 2-4, 6 and 9-11 made in paragraph 18(f) of the Office Action mailed 07/27/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims and/or the base claim.

15) The rejection of claim 10 made in paragraph 18(g) of the Office Action mailed 07/27/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

16) The rejection of claim 42 made in paragraph 18(h) of the Office Action mailed 07/27/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

17) The rejection of claims 2-11, 43-46 and 52 made in paragraph 18(i) of the Office Action mailed 07/27/07 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claims.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

18) Claim 42 and the dependent claims 43-45 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 42, as amended, includes the following new limitations: 'a pharmaceutically acceptable carrier and multivalent conjugate molecules, wherein each multivalent conjugate molecule comprises a ….. wherein each type of said at least three different types of purified bacterial capsular polysaccharides is obtained from a different serotype of a bacteria by treating the bacteria with an enzyme or base, directly followed by separation to isolate said at least three

different types of purified bacterial capsular polysaccharide and .... multivalent conjugate molecules' [Emphasis added]. The currently recited multivalent conjugate molecules encompass a mixture of such conjugate molecules wherein one conjugate molecule contains, for example, GBS Ia, III and V capsular polysaccharides covalently linked to C-beta protein; second conjugate molecule contains, for example, pneumococcal 6, 7 and 19F capsular polysaccharides covalently linked to tetanus toxoid, etc, wherein the capsular polysaccharides are obtained as recited in the amended claim 42. Applicants point to paragraph [67] of the specification and state that this part of the specification provides support for the 'conjugate molecules of the invention ... typically administered as a pharmaceutical composition in a pharmaceutically acceptable carrier'. Applicants also point to paragraph [87] of the specification allegedly showing that one dose for a CD1 female mouse is 1 microgram of conjugated-type polysaccharide, which 'must' contain more than one conjugate molecule. However, neither paragraph [67] nor paragraph [87] is supportive of a pharmaceutical composition comprising 'multivalent conjugate molecules', wherein each multivalent conjugate molecule comprises a carrier protein with at least three different types of purified bacterial capsular polysaccharides, as claimed in the amended claim 42, wherein the multivalent conjugate *molecules* are present in an amount 'sufficient to elicit protective antibodies' against the three different types of bacterial capsular polysaccharides. Paragraph 87 of the specification is reproduced below which is not supportive of the now recited limitations and the now claimed scope of claim 42:

> [87] The multivalent conjugate was tested for the ability to elicit a protective immune response. The efficacy of the tetravalent chimeric conjugate prepared as described herein was evaluated in comparison to a tetravalent vaccine mixture comprising, a Ia/Ib/III/V combination vaccine, i.e., a mixture of monovalent conjugates. Animals (CD 1 female mice) were inoculated with the chimeric vaccine or the combination tetravalent vaccine mix. Each animal received 1 mg of each of the conjugated type-polysaccharide, at days 0 and 21. Vaccines were adsorbed on Aluminum hydroxide (Superfos, Denmark). Mice were impregnated at day 21. Neonates were challenged 48 hours following birth with GBS type Ia, GBS type Ib, GBS tpe III or GBS type V. The results (Figure 11) show that the chimeric conjugate was as effective as the tetravalent vaccine mixture in eliciting a protective immune response.

Thus, paragraph [87] describes the induction of protective immune response of a tetravalent chimeric vaccine, i.e., a mixture of *monovalent* conjugates. Therefore, the above-identified limitations in the claim(s) are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter

but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to specific pages and lines that provide the descriptive support in the specification as originally filed, for the above-identified new limitations, or alternatively, remove the new matter from the claim(s). See MPEP 714.02 and 2163.06.

19) Claims 1-11, 42-46 and 52 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1 and 42, as amended, include the limitations: 'different types of purified bacterial capsular polysaccharide … wherein each type of said at least three different types of purified bacterial capsular polysaccharide is obtained from a different serotype of a bacteria by treating the bacteria with an enzyme or base, directly followed by separation to isolate said at least three different types of purified bacterial capsular polysaccharide'. Claims 2-4 and 6, as amended, also include the new limitation 'different types of purified bacterial capsular polysaccharide'. The generic limitation 'different types of purified bacterial capsular polysaccharide' encompasses, for example, O-acetylated purified bacterial capsular polysaccharide, non-O-acetylated purified bacterial capsular polysaccharide, and de-N-acetylated purified bacterial capsular polysaccharide types resulting from base treatment. Applicants point to paragraphs [02], [77] to [80], [06], [56], [57], [67] and [87] of the specification and state that these parts provide support for the claim amendments. However, the specification lacks descriptive support for 'different types' of purified bacterial capsular polysaccharide. Furthermore, the specification lacks support for the limitation '*directly* followed by separation to *isolate* said ….. different types of *purified* bacterial capsular polysaccharide' [Emphasis added]. Treatment of the bacteria with an enzyme or base directly followed by separation would be expected to result in an isolated capsular polysaccharide, but not a purified capsular polysaccharide. Therefore, the above-identified limitations in the claim(s) are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter

but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to specific pages and lines that provide the descriptive support in the specification as originally filed, for the above-identified new limitations, or alternatively, remove the new matter from the claim(s). See MPEP 714.02 and 2163.06.

20) Claim 52 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 52, as amended, includes the new limitations: purified polysaccharides 'having a molecular weight of *100 kilodaltons or less*' [Emphasis added]. Applicants state that support for this amendment can be found at paragraph [41] of the specification, which allegedly describes 'the purified *oligosaccharide*' as 'substantially free of intact polysaccharide capsule, or fragments of it having a *molecular weight above 100,000*' [Emphasis added]. Clearly, paragraph [41] of the specification does not provide descriptive support for purified *polysaccharides* having a molecular weight of *100 kilodaltons or less*' because a 'purified oligosaccharide' 'or bacterial capsule polysaccharide' that is substantially free of intact polysaccharide capsule or fragments of it having a molecular weight 'above 100,000' does not have *any* molecular weight limit. The limitation 'substantially free of intact polysaccharide capsule or fragments of it having a molecular weight 'above 100,000' at paragraph 41 does not place a molecular weight limit on the recited 'purified polysaccharides'. Therefore, the above-identified limitations in the claim(s) are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to specific pages and lines that provide the descriptive support in the specification as originally filed, for the above-identified new

limitations, or alternatively, remove the new matter from the claim(s). See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

21) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

22) Claims 1-11, 42-46 and 52 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 42 is indefinite, confusing, and internally inconsistent in the limitations: 'purified capsular polysaccharides' (see line 5) and 'purified bacterial capsular polysaccharide' (see line 9).

(b) Claim 42 lacks proper antecedent basis in the limitations: 'purified bacterial capsular' (see lines 6 and 9). Since the earlier part of the claim already includes the limitation, it is suggested that Applicants provide proper antecedent basis by replacing the limitation with --the purified capsular--.

(c) Claim 42 is indefinite, confusing, and inconsistent in the limitations: 'at least three types of purified capsular polysaccharides' (see lines 6 and 7) and 'the three different types of bacterial capsular polysaccharides' (see last two lines). Is the latter purified or not? Furthermore, the 'at least' has no upper limit and therefore, the scope of the limitation 'at least three' is not the same as the scope of the limitation 'the three'.

(d) Claims 2-4, as amended, are indefinite and confusing in the limitation: 'different types of bacterial capsular polysaccharide constitute .... said ... different types of purified bacterial capsular polysaccharide'. The limitation 'different types of bacterial capsular polysaccharide' encompasses unpurified bacterial capsular polysaccharides. It is unclear how such unpurified bacterial capsular polysaccharides constitute purified bacterial capsular polysaccharide.

(e) Claim 6 is inconsistent and/or lacks proper antecedent basis in the limitations: 'bacterial capsular polysaccharides' (see line 1) [Emphasis added]. Claim 6 depends from claim 1, which recites '*purified* bacterial capsular polysaccharide'.

(f) Claim 44 is indefinite in the limitation 'the bacterial capsular polysaccharides', because it is unclear where this limitation derives its antecedence from. Claim 44 depends from claim 42, which includes the limitations (a) 'purified capsular polysaccharides' and (b) 'bacterial capsular polysaccharides'. Are 'the bacterial capsular polysaccharides' recited in claim 44 purified or unpurified?

(g) Claim 52 is indefinite, confusing and appears to be improperly broadening in scope in the limitation: 'the polysaccharides are purified polysaccharides'. Claim 52 depends from claim 1 which is limited to 'purified bacterial capsular polysaccharide'. Claim 1 from which claim 52 depends does not include the plural limitation 'polysaccharides'.

(h) Claims 9-11 are indefinite and appear to have improper antecedent basis in the limitation: 'the bacterial capsular polysaccharides' [Emphasis added]. Claims 9-11 depend indirectly from claim 1, which includes the limitation 'bacterial capsular polysaccharide', but not 'bacterial capsular polysaccharides'.

(i) Claim 11 is not properly limiting in the limitation: 'the bacterial capsular polysaccharides'. Claim 10 depends from claim 6 wherein 'the .... bacterial capsular polysaccharides' are already limited to 'different Group B Streptococcus capsular polysaccharides'. It is suggested that Applicants replace the above-identified limitation with the limitation --the different Group B *Streptococcus* capsular polysaccharides--.

(j) Claims 2-11, 43-46 and 52, which depend from claim 1 or claim 42, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 103

23) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

24) Claims 1, 2, 5, 6, 10, 11, 42 and 44 are rejected under 35 U.S.C § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, already of record) in view of Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, already of record) (Paoletti *et al.*, 1994).

It is noted that the 'protective antibodies' recited in the independent claims do not exclude anti-carrier protein protective antibodies.

Chong *et al.* disclosed a multivalent immunogenic conjugate molecule comprising a carrier protein such as tetanus toxoid and multiple different purified carbohydrate fragments each linked to the carrier protein and a vaccine comprising the same in a physiologically acceptable carrier. See claims 12, 11, 2 and 1; and paragraphs [0091] to [0095]. Chong *et al.* taught a novel glycoconjugate technology that can be used to covalently link multiple oligosaccharides from Group B *Streptococcus* 'to the same carrier protein' and the multivalent conjugate molecules produced thereby. See section [0057]. The conjugate components are present in equimolar amounts and induce anti-carrier antibodies. See section [0084]. Chong's multivalent immunogenic conjugate molecule is expected to elicit anti-tetanus toxoid antibodies that are known in the art to be protective.

Chong *et al.* do not expressly identify Group B *Streptococcus* to be types to be type Ia, type III and type V capsular types.

However, Paoletti *et al.* (1994) taught at least four different purified types Ia, Ib, II and III of Group B *Streptococcus* capsular polysaccharides, which were purified according to reference 32 cited therein and which elicited protective antibodies against the capsular polysaccharides as evaluated using a mouse maternal immunization-neonatal challenge model of GBS infection, upon covalent linking to tetanus toxoid via 7-29% of the sialic acid residues oxidized. Paoletti *et al.* (1994) taught a method of producing individual monovalent GBS type capsular

polysaccharide-protein conjugates and combining the monovalent conjugates to produce a tetravalent conjugate vaccine. See abstract; Materials and Methods; Tables 1, 2, 5 and 6; Figure 1; and pages 3237 and 3238.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a multivalent conjugate molecule by covalently linking Paoletti's four different purified, protective types Ia, Ib, II and III Group B *Streptococcus* capsular polysaccharides to the 'to the same carrier protein' such as Chong's tetanus toxoid using Chong's novel glycoconjugate technology to produce the instant invention with a reasonable expectation of success. Given Chong's express teaching or suggestion that their novel glycoconjugate technology can be used to covalently link multiple oligosaccharides from Group B *Streptococcus* to the same carrier protein, one of ordinary skill in the art would have been motivated to produce the instant invention because one of ordinary skill in the art would have readily recognized that Chong's novel glycoconjugate technology is less time-consuming, more economical involving lesser steps, and includes steps that avoid cumbersome mixing of individual conjugate products.

Claims 1, 2, 5, 6, 10, 11, 42 and 44 are *prima facie* obvious over the prior art of record.

25) Claims 9 and 52 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, already of record) as modified by Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, already of record) (Paoletti *et al.*, 1994) as applied to claims 1 and 6 above, and further in view of Wang *et al.* (*PNAS* 95: 6584-6589, 1998, already of record).

The teachings of Chong *et al.* as modified by Paoletti *et al.* (1994) are explained above which do not expressly teach that the capsular polysaccharides in their glycoconjugate are of a size between 80 and 120 kilodaltons or less than 100 kilodaltons.

However, the depolymerised GBS capsular polysaccharides of desired size, including those that fall in the range between 80 and 120 kilodaltons, or less than 100 kilodaltons and a method of making them were known in the art at the time of the invention. For instance, Wang *et al.* taught the selectively depolymerised GBS types I-VIII capsular polysaccharides of desired size obtained by controlled treatment of the full-length capsular polysaccharides with ozone, without affecting the labile sialic acid residues of the polysaccharides. A specific sized capsular polysaccharide obtained was of the size 61 kDa. Wang *et al.* taught of the art-known, frequently

proven preference for short-chain polymers or oligomer fragments of capsular polysaccharides of pathogenic microorganisms including Group B *Streptococci,* for use in vaccine applications. See abstract; 'Materials and Methods'; section 'Kinetics' on page 6587; first paragraph under 'Results and Discussion'; and left column on page 6584; and page 6588.

Given that depolymerised capsular polysaccharides of GBS types having a size of 61 kDa and having the intact or unaffected sialic acid residues were already known in the art at the time of the invention as taught by Wang *et al.*, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to replace the GBS capsular polysaccharides of types Ia, Ib, II and III in Chong's multivalent GBS conjugate vaccine as modified by Paoletti *et al.* with Wang's depolymerised GBS capsular polysaccharides of types Ia, Ib, II and III to produce the multivalent conjugate of the instant invention, with a reasonable expectation of success. Given the frequently proven preference for short-chain polymers or oligomer fragments of capsular polysaccharides of pathogenic microorganisms including Group B *Streptococci* for application in vaccines as taught by Wang *et al.*, one of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a multivalent GBS capsular polysaccharide conjugate for application in vaccines.

Claims 9 and 52 are *prima facie* obvious over the prior art of record.

26) Claims 3 and 4 are rejected under 35 U.S.C. § 103(a) as being unpatentable over 35 U.S.C. § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, already of record) as modified by Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, already of record) (Paoletti *et al.*, 1994) as applied to claims 1 and 6 above, and further in view of Paoletti *et al.* (*J. Infect. Dis.* 180: 892-895, 1999).

The teachings of Chong *et al.* as modified by Paoletti *et al.* (1994) are explained above which do not teach the number of different types of purified GBS capsular polysaccharides to be five or six.

However, additional purified GBS type VI and type VIII capsular polysaccharides and the importance of including these types in a conjugate vaccine were known in the art at the time of the invention. For example, Paoletti *et al.* (1999) taught that GBS types VI and VIII are prevalent serotypes isolated from pregnant women in Japan. Paoletti *et al.* (1999) taught purified capsular

polysaccharides of GBS types VI and VIII which upon conjugation induced protective antibodies. Paoletti *et al.* (1999) expressly suggested GBS types VI and VIII conjugate vaccines to be important components of a multivalent GBS vaccine for use in regions where these serotypes are predominate. See abstract; Materials and Methods; and Results.

Given Paoletti's (1999) express teaching that GBS types VI and VIII are prevalent serotypes isolated from pregnant women in Japan, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include Paoletti's (1999) purified type VI and type VIII capsular polysaccharides along with Paoletti's (1994) purified protective types Ia, Ib, II and III Group B *Streptococcus* capsular polysaccharides while conjugating to Chong's tetanus toxoid using Chong's novel glycoconjugate technology to produce the instant invention with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a multivalent GBS vaccine that includes these two GBS types for use in regions where these serotypes are predominate as taught by Paoletti *et al.* (1999).

Claims 3 and 4 are *prima facie* obvious over the prior art of record.

27) Claims 7 and 45 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, already of record) as modified by Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, already of record) (Paoletti *et al.*, 1994) as applied to claims 6 and 44 above, and further in view of Wessels *et al.* (*J. Infect. Dis.* 171: 879-884, 1995, abstract).

The teachings of Chong *et al.* as modified by Paoletti *et al.* (1994) are explained above which do not teach type V GBS purified polysaccharide to be a part of their multivalent conjugate molecule.

However, Wessels *et al.* taught of the recognition in the art of type V strains of GBS as frequent cause of GBS infections in both infants and adults. Wessels *et al.* taught purified GBS V capsular polysaccharide and showed that it produces protective antibodies on conjugation to a protein. Wessels *et al.* (1995) expressly suggested the inclusion of type V GBS conjugate in a multivalent GBS vaccine for human use. See abstract.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include Wessel's purified type V GBS capsular polysaccharide along with

Paoletti's (1994) purified protective types Ia, Ib, II and III Group B *Streptococcus* capsular polysaccharides while conjugating to Chong's tetanus toxoid using Chong's novel glycoconjugate technology to produce the instant invention with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a multivalent GBS vaccine that includes type V capsular polysaccharide for use in humans in whom type V GBS is a frequent cause of GBS infections as taught by Wessels *et al.*

Claims 7 and 45 are *prima facie* obvious over the prior art of record.

28) Claims 8 and 46 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chong *et al.* (US 2001/0048929, already of record) as modified by Paoletti *et al.* (*Infect. Immun.* 62: 3236-3243, 1994, already of record) (Paoletti *et al.*, 199 4), Wessels *et al.* (*J. Infect. Dis.* 171: 879-884, 1995) as applied to claims 7 and 45 above, and further in view of Michon *et al.* (*In: Streptococci and the Host.* (Ed) Horaud *et al.* Plenum Press, New York, pages 847-850, 1997, already of record) (Michon *et al.*, 1997) and Laude-Sharp *et al.* (*In: Abstracts of the 97th General Meeting of the American Society for Microbiology*, Miami Beach, FL, page 251, # E-62, 1997, already of record).

The teachings of Chong *et al.* as modified by Paoletti *et al.* (1994) and Wessels *et al.* are explained above which do not teach the carrier protein to be C beta protein.

However, the use of C beta protein as a protein carrier in a multivalent GBS capsular polysaccharide conjugate was known in the art at the time of the invention. For instance, Michon *et al.* (1997) disclosed the use of C protein carrier as an alternative to tetanus toxoid protein carrier in producing a multivalent GBS capsular polysaccharide conjugate. Michon *et al.* (1997) taught that beta C protein is a good carrier protein whose conjugation to different GBS type capsular polysaccharides does not alter its antigenicity. See sections 1 and 4.

Laude-Sharp *et al.* taught the advantages of using streptococcal C-beta protein as a carrier protein in a combination conjugate vaccine against multiple serotypes of Group B *Streptococcus*. Laude-Sharp *et al.* conjugated the streptococcal C-beta protein to the capsular polysaccharides of different types of GBS and showed that besides its carrier function, the C beta protein afforded protection against GBS strains not covered by capsular polysaccharides in the vaccine. In

addition to providing protection against different GBS types used, the conjugate vaccine provided additional protection against GBS type Ib. See title and entire disclosure.

Given Michon's (1997) express teaching that beta C protein is a good carrier protein whose conjugation to different GBS type capsular polysaccharides does not alter its antigenicity, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to replace tetanus toxoid protein carrier in Chong's multivalent GBS conjugate as modified by Paoletti *et al.* (1994) and Wessels *et al.* with Michon's (1997) C beta protein to produce the instant invention with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of producing a multivalent GBS conjugate vaccine wherein five different GBS type capsular polysaccharides are conjugated to streptococcal beta C protein, which multivalent conjugate not only advantageously confers immunity against multiple GBS types, but also affords protection via C-beta protein against GBS strains not covered by the capsular polysaccharides in the vaccine and provides additional protection against GBS type Ib as taught by Laude-Sharp *et al.*

Claims 8 and 46 are *prima facie* obvious over the prior art of record.

Remarks

29) Claims 1-11, 42-46 and 52 stand rejected.

30) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted to the Office' Central Rightfax number 571-273-8300 via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week.

31) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

32) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Shanon Foley, can be reached on (571) 272-0898.

/S. Devi/
S. Devi, Ph.D.
Primary Examiner
AU 1645

May, 2008